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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/543,048	01/26/2006	Philipp Hadwiger	26421-15811 US	3878
77328 ALNYLAM/FE	7590 03/11/201 ENWICK	EXAMINER		
SILICON VAL 801 CALIFORI		CHONG, KIMBERLY		
	YIEW, CA 94041	ART UNIT	PAPER NUMBER	
			1635	
			NOTIFICATION DATE	DELIVERY MODE
			03/11/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Advisory Action Before the Filing of an Appeal Brief

Application No.	Applicant(s)	
10/543,048	HADWIGER ET AL.	
Examiner	Art Unit	

	KIMBERLY CHONG	1635	
The MAILING DATE of this communication appe	ars on the cover sheet with the c	correspondence add	ress
THE REPLY FILED <u>12 February 2010</u> FAILS TO PLACE THIS A	APPLICATION IN CONDITION FO	R ALLOWANCE.	
1. The reply was filed after a final rejection, but prior to or on application, applicant must timely file one of the following application in condition for allowance; (2) a Notice of Appe for Continued Examination (RCE) in compliance with 37 C periods:	replies: (1) an amendment, affidaviral (with appeal fee) in compliance	t, or other evidence, w with 37 CFR 41.31; or	hich places the (3) a Request
 a) The period for reply expires 3 months from the mailing date b) The period for reply expires on: (1) the mailing date of this Are no event, however, will the statutory period for reply expire la 	dvisory Action, or (2) the date set forth		
Examiner Note: If box 1 is checked, check either box (a) or (I MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f Extensions of time may be obtained under 37 CFR 1.136(a). The date of the control of the).		
have been filed is the date for purposes of determining the period of ext under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the s set forth in (b) above, if checked. Any reply received by the Office later may reduce any earned patent term adjustment. See 37 CFR 1.704(b). NOTICE OF APPEAL	ension and the corresponding amount of the hortened statutory period for reply origi	of the fee. The appropria nally set in the final Offic	ate extension fee e action; or (2) as
2. The Notice of Appeal was filed on A brief in complifiling the Notice of Appeal (37 CFR 41.37(a)), or any exter Notice of Appeal has been filed, any reply must be filed wi	sion thereof (37 CFR 41.37(e)), to	avoid dismissal of the	
AMENDMENTS			
 The proposed amendment(s) filed after a final rejection, be (a) They raise new issues that would require further core (b) They raise the issue of new matter (see NOTE below 	sideration and/or search (see NO		cause
(c) They have not deemed to place the application in bett appeal; and/or	•	ducing or simplifying t	ne issues for
(d) ☐ They present additional claims without canceling a converse NOTE: (See 37 CFR 1.116 and 41.33(a)).	orresponding number of finally reje	ected claims.	
4. The amendments are not in compliance with 37 CFR 1.12	21. See attached Notice of Non-Co	mpliant Amendment (PTOL-324).
5. Applicant's reply has overcome the following rejection(s):			,
 Newly proposed or amended claim(s) would be all non-allowable claim(s). 	-	imely filed amendmer	nt canceling the
7. For purposes of appeal, the proposed amendment(s): a) [how the new or amended claims would be rejected is prov The status of the claim(s) is (or will be) as follows: Claim(s) allowed: Claim(s) objected to: Claim(s) rejected: Claim(s) withdrawn from consideration:		l be entered and an e	xplanation of
AFFIDAVIT OR OTHER EVIDENCE			
 The affidavit or other evidence filed after a final action, but because applicant failed to provide a showing of good and was not earlier presented. See 37 CFR 1.116(e). 			
9. The affidavit or other evidence filed after the date of filing a entered because the affidavit or other evidence failed to or showing a good and sufficient reasons why it is necessary	vercome <u>all</u> rejections under appea	ıl and/or appellant fail	s to provide a
10. ☐ The affidavit or other evidence is entered. An explanation REQUEST FOR RECONSIDERATION/OTHER	n of the status of the claims after er	ntry is below or attach	ed.
 The request for reconsideration has been considered but <u>See Continuation Sheet.</u> 	does NOT place the application in	condition for allowan	ce because:
12. ☐ Note the attached Information <i>Disclosure Statement</i>(s). (13. ☐ Other:	PTO/SB/08) Paper No(s)		
	/Kimberly Chong/ Primary Examiner AU16	35	

Continuation of 11. does NOT place the application in condition for allowance because: Applicant's arguments do not overcome the rejections of record. Applicant continues to argue that Rana continues to tegach the importance and necessity of the 5' end hydroxyl of the antisense strand of an siRNA for RNAi activity. First it must be pointed out that Rana has not been used as a prior art reference in the 103 rejection of record. Applicant appears to use Rana as evidence that the prior art teach that the 5' end of the antisense strand should contain a free OH group. The prior art demonstrates that as long as the 5' end of the antisense strand contains a phosphate group, the dsRNA appears to remain amenable to RNAi as demonstrated by Schwarz et al. who teach a dsRNA wherein the 5' end was linkd with a phosphodiester linkage. Applicant did not address the Schwarz et al. reference as evidence of what was taught in the prior art. Thus because Rana was not used in the rejection of record as motivation to not modify the 5' end of an antisense strand of a dsRNA and because it was known in the prior art that a dsRNA containing a phosphodiester group at the 5 end was amendable to RNAi, this argument is not persuasive. Applicant argues Fosnaugh et al. teach too many variatins and one would not arrive at the claimed invention with a reasonable expectation of success. As stated previously, given there are a finte number of identified predicatable solutions for attaching a lipophilic grop to either of 4 positions of a dsRNA, a skilled artisan would have a good reason to modified said dsRNA with a reasonable expectation of success. The claimed dsRNA broadly recites attached any lipophilic group to the 5' end wherein the 5' end comprises a phosphodiester group and does not recite any unexpected results that would make the claimed invention non-obvious to the skilled artisan. Lastly Applicant argues Florence does not teach the claimed logKow value because both describe the log of the partition coefficient and that these terms are the same and therefore Florence teach the log as 1.24 which is not the claimed log of greater than 1.5. This is not persasive because Florence was cited for teach a conjugate with a partition coefficient of a certain value and as explained in the instant specification, the lipophilic group is defined by the partition coefficient. There is nothing in either the specification or Florence that defines the log P and logKow as equivalent. Thus the rejections of record are maintained.